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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,027	10/27/2000	Jonathan L. Sessler	4201.01 US	6781

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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/699,027	SESSLER ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-19,22,23 and 25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20 and 21* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the response filed 3/16/04, claim 20 has been amended. Claims 1-27 remain pending. Claims 1-19, 22, 23, 25-27 remain withdrawn from consideration Claims 20, 21, 24 are examined in this Office action.

Applicants' arguments filed 3/16/04 have been considered and found persuasive in part. The rejection of claim 20 as unpatentable over Sessler ('946) in view of Lehninger (Biochemistry, pages 641-642) is withdrawn.

Claim 24 is objected to because of its dependence on rejected claims.

❀

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

❀

Claim 20 is rejected under 35 U.S.C. §103 as being unpatentable over Sessler (USP 5,622,946) in view of Lehninger (Biochemistry, 2nd Edition, pages 503-504; Worth Publishers, 1975).

As indicated previously, Sessler discloses a method of inducing oxidative stress by administering a compound that meets the requirements of instant claim 20, step (a). Sessler does not explicitly disclose that the patient should be allowed to breathe air, nor does Sessler disclose that molecular oxygen is a cellular metabolite.

Lehninger discloses that molecular oxygen is a cellular metabolite; it is produced, for example, by superoxide dismutase, and by catalase. Lehninger does not disclose a method for inducing targeted oxidative stress.

The response (filed 3/16/04) argues that (a) claim 20 does not require ionizing radiation, and (b) claim 20 does not permit ionizing radiation. While it is true that claim 20 does not require ionizing radiation, it is incorrect to suggest that claim 20 does not permit ionizing radiation. Claim 20 is drawn to a method that "comprises" the indicated steps; as such, additional steps are encompassed. Claim 20 does not exclude the additional step of administering ionizing radiation.

The response (filed 3/16/04) also argues that the term "cellular metabolite" is described

(p. 18, specification) as referring to compounds which have a reduction potential which is more negative than that of molecular oxygen. While there may be such a description in the specification, there is no such limitation in any of the elected claims. It is noted that such a limitation is present in (non-elected) claim 1. However, it is appropriate to interpret the term "cellular metabolite" as broadly as a biochemist of ordinary skill would interpret the term. The term "cellular metabolite", without further qualification, would encompass any molecule produced by a cell. A variety of prokaryotic and eukaryotic cells produce oxygen; even mammals produce this molecule. Given that the claims impose no limits on oxidation potential, the instant claims encompass molecular oxygen as the cellular metabolite. The response further argues that the specification provides examples of cellular metabolites, and that among the list of possibilities, molecular oxygen is not included. However, claim 20 does not recite any specific cellular metabolite, and so all such metabolites would be encompassed.

The rejection is maintained.

❀

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Vogel (USP 5,244,671).

As indicated previously, Vogel disclose the use of photactivatable porphycenes. Also disclosed (e.g., col 6, line 66) is the production of singlet oxygen following irradiation. Also

disclosed (col 7, line 32) is the co-adminstration of ascorbic acid.

The response filed 3/16/04 argues that the porphycenes of Vogel are not the same as the texaphyrins of the claimed invention, since the term "texaphyrin" is such as to require the presence of a metal ion. However, the term "texaphyrin", without further qualification, does not preclude the absence of a metal ion, just as the term "porphyrin", without further qualification, does not require the presence of a metal ion. But in any case, neither of claims 20 or 21 makes any mention of texaphyrins. What is required is "an agent that preferentially accumulates in tumor... and catalyses the production of ...reactive oxygen species...". Vogel does disclose that the compounds accumulate in tumors. Also disclosed (col 11, line 27+; col 11, line 42+) is that the porphycenes produce singlet oxygen which is the agent that destroys neoplastic cells. Thus, the examiner maintains that "porphycenes" fall within the scope of the term "texaphyrin", but even if "texaphyrins" do not include "porphycenes", the point is moot, since the rejected claims make no mention of texaphyrins.

The response filed 3/16/04 also argues that the intended use of the ascorbic acid in Vogel is different from the intended use of ascorbic acid in the instant claims. While this may be true, the fact of this (or the possibility of this) is not reflected in the instant claims. The preferred "cellular metabolite" is ascorbic acid, and the reference discloses administration of this. Whatever effects ascorbic acid will have in the hands of a

practitioner of the claimed invention will be the same as ascorbic acid will have in the hands of a practitioner of the Vogel invention. The response also points to Magda (*Chem Commun* 2730, 2002) which shows that when motexafin gadolinium is combined with ascorbic acid in the presence of oxygen, spectral changes occur which can be explained by the formation of an oxalate complex of the motexafin gadolinium. The response argues that "production of reactive oxygen species cannot aid in maintaining chemical stability". This particular statement may very well be true, but its relevance to the instant claims is not made clear. The examiner has not argued that the porphycenes of Vogel will react with ascorbic acid to produce the complex observed by Magda. However, (a) the rejected claims do not require the use of motexafin, or any other texaphyrin, and (b) the rejected claims make no mention of the oxalate complex observed by Magda. The claims, in fact, neither require the "cellular metabolite" to react with the "agent" of step (a) nor exclude any such reaction. Thus, while there may be differences between the chemical reactivity of motexafin and the Vogel compounds, such differences are not reflected in the instant claims.

The response also argues that the claimed invention is distinguished over Vogel in that Vogel requires ionizing radiation, whereas claim 20 does not require ionizing radiation. However, claim 20 does permit ionizing radiation, and so the claimed invention is not distinguished on this basis.

The rejection is maintained.

❀

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Vogel (USP 5,244,671) in view of Kimoto (*Cancer Research* **43** (2) 824-8, 1983) or Bram (*Nature* 284 (5757) 629-31, 1980).

The teachings of Vogel were indicated previously. Vogel does not disclose that ascorbic acid will enhance the anticancer activity of the Vogel compounds. Kimoto and Bram disclose that ascorbic acid is an anticancer agent in the presence of oxygen. Thus, the practitioner of the Vogel invention would recognize that the ascorbic acid will produce additive effects in the treatment of cancer.

The response (filed 3/16/04) argues that the inventions of Kimoto and of Bram are "different" from that which is claimed. In particular (it is argued), Kimoto requires cupric ions, whereas the claimed invention does not. However, the instant claims do not exclude cupric ions. The claimed method "comprises" the three indicated steps, and as such, the presence of cupric ions (as well as any number of other agents) is encompassed. In reference to Bram, the response also argues that cupric ions are required. Again, cupric ions are not excluded by the instant claims. The response further argues that "one skilled in the art would not be motivated to use texaphyrins...". The examiner maintains that the Vogel compounds fall within the scope of the term "texaphyrin", but even

if this weren't true, the rejected claims make no mention of texaphyrins. The question of motivation to use texaphyrins is thus moot.

The rejection is maintained.

❀

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Platzek (USP 6,136,841).

Platzek discloses the use of porphyrins for photodynamic therapy. Also disclosed (col 7, line 57) is the co-administration of the porphyrin with ascorbic acid.

The response filed 3/16/04 argues that Platzek requires irradiation, whereas irradiation is not required by claim 20. While this is true, it is also true that claim 20 permits irradition, since claim 20 "comprises" several process steps, and as such, additional process steps are included.

The rejection is maintained.

❀

Claims 20 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Platzek (USP 6,136,841) in view of Kimoto (*Cancer Research* **43** (2) 824-8, 1983) or Bram (*Nature* 284 (5757) 629-31, 1980).

The teachings of Platzek were indicated previously. Platzek does not disclose that ascorbic acid will enhance the anticancer activity of the Platzek compounds. Kimoto and

Bram disclose that ascorbic acid is an anticancer agent in the presence of oxygen. Thus, the practioner of the Platzek invention would recognize that the ascorbic acid will produce additive effects in the treatment of cancer.

The response filed 3/16/04 argues that claim 20 does not require irradiation, whereas the invention of Platzek does require irradiation. However, claim 20 does permit irradiation, and so the claimed invention is not distinguished (from the cited references) on this basis. The response also states that Kimoto and Bram both require copper ions, and the response implies that the use of copper ions is excluded from the claims. However, the claims comprise the recited steps, and as such do not preclude the use of copper ions. The response also argues that the reference do not teach the use of texaphyrins in combination with ascorbic acid. However, the rejected claims do not require the use of texaphyrins, and so the claimed invention is not distinguished on this basis.

The rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED

UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton 5/24/04

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